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Docket No. GJE-89
Serial No. 10/089,877In the Claims

1-21 (canceled)

22 (currently amended). A method for determining the sequence of a polynucleotide, comprising the steps of:

- i. reacting a target polynucleotide with an enzyme that interacts with and processes along the polynucleotide, under conditions sufficient to induce enzyme activity; and
- ii. detecting conformational changes in the enzyme as the enzyme processes along the polynucleotide, and thereby determining the sequence of the polynucleotide;

wherein the enzyme comprises a first bound fluorescent molecule, the characteristics of which alter as the enzyme undergoes a conformational change, and wherein the target polynucleotide does not comprise a label prior to, during, or after the enzyme processes along the polynucleotide, and wherein if step (i) is carried out in the presence of nucleotide monomers, the nucleotide monomers do not comprise a label.

23 (previously presented). The method according to claim 22, wherein the enzyme is a polymerase enzyme.

24 (previously presented). The method according to claim 22, wherein the enzyme is a helicase enzyme or a primase enzyme.

25 (previously presented). The method according to claim 22, wherein the enzyme is immobilised on a solid support.

26 (previously presented). The method according to claim 25, comprising a plurality of enzymes immobilised on the solid support.

27 (canceled).

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28 (currently amended). The method according to claim 22, wherein the enzyme comprises a bound label that interacts with the first bound fluorescent molecule, wherein the degree of interaction is dependent on a conformational change in the enzyme.

29 (canceled).

30 (currently amended). The method according to claim 28, wherein the first bound fluorescent molecule is an energy acceptor and the bound label is an energy donor, or wherein the first bound fluorescent molecule is an energy donor and the bound label is an energy acceptor, and wherein step (ii) is carried out by measuring energy transfer between the first bound fluorescent molecule and the bound label.

31 (canceled).

32 (previously presented). The method according to claim 22, wherein step (ii) is carried out using confocal microscopy.

33 (previously presented). The method according to claim 32, wherein step (ii) is carried out by fluorescence imaging.

34 (currently amended). The method according to claim 22, wherein step (ii) is carried out by measuring a polarisation effect consequent on the altered characteristics of the first bound fluorescent molecule.

35 (previously presented). The method according to claim 34, wherein step (ii) is carried out by fluorescence polarisation anisotropy.

36-40 (canceled).

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41 (currently amended). A solid support comprising at least one immobilised polymerase or helicase enzyme, the enzyme being labelled with at least one fluorescence resonance energy transfer (FRET) FRET donor label and at least one FRET acceptor label.

42 (canceled).

43 (currently amended). The solid support according to claim 41, wherein the at least one FRET fluorescence resonance energy transfer donor label is a fluorophore.

44 (canceled).

45 (currently amended). A system for determining a sequence of a polynucleotide, comprising a solid support ~~according to claim 41~~ comprising at least one immobilised polymerase or helicase enzyme, the enzyme being labelled with at least one fluorescence resonance energy transfer (FRET) donor label and at least one FRET acceptor label, and an apparatus for detecting the label.

46 (currently amended). The solid support according to claim 41, wherein the at least one FRET fluorescence resonance energy transfer acceptor label is a fluorophore.

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